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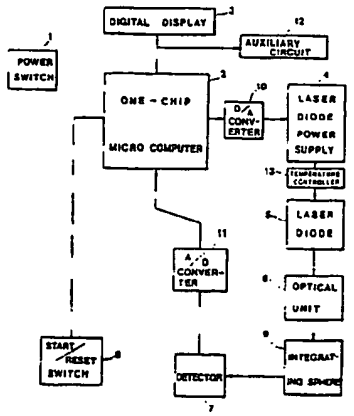
(54) A non-invasive method and apparatus for measuring blood chemical concentration.

(57) A method and apparatus for measuring blood glucose concentration by irraditing blood vessels with electromagnetic radiation using near-infrared radiation diffuse-reflection laser spectroscopy. This invention uses electromagnetic radiation of a wavelength that is transmitted through the skin to the measurement part, for example, a blood vessel. Since skin is mostly composed of water (H_2O), which absorbs IR radiation in nearly the entire IR spectral range, only radiation of a certain, narrow protion of the IR spectral range called the "water transmission window" is transmitted through the skin. The present invention uses electromagnetic radiation with a wavelength of 1.3μm~1.9μm radiation from a semiconductor diode laser (5). When electromagnetic radiation of these wavelengths irradiates the skin, light is transmitted through the skin to the blood vessel where the light interacts with the heterogeneous components of the blood. The light which reaches the blood is then diffusely reflected by the blood. The reflected light will have been modulated by the characteristic vibrations of the molecules which are major components of blood. The reflected light is detected and provided as a digital signal to a one-chip microcomputer (2). The one-chip microcomputer (2) calculates a blood glucose concentration from the digital signal by reference to a calibration curve stored in the memory of the one-chip microcomputer (2). The one-chip microcomputer (2) causes the calculated blood glucose concentration to be displayed on a digital display (3).

FIG.1.



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A NON-INVASIVE METHOD AND APPARATUS FOR MEASURING BLOOD CHEMICAL CONCENTRATION

BACKGROUND OF THE INVENTION

FIELD OF THE INVENTION

The present invention relates to a method and apparatus for measuring blood chemical concentration, and more particularly, to a non-invasive technique for measuring eg blood glucose concentration using near-infrared radiation diffuse-reflection laser spectroscopy.

PRIOR ART

Generally, diabetics measure blood glucose concentration two to eight times daily using a portable measurement apparatus consisting of an injector (to obtain a blood sample) and test paper (to measure the amount of glucose in the blood). This is known as the "enzymatic" method or test.

The enzymatic test for glucose concentration is undesirable both because it requires that blood be drawn and because it is expensive. Less expensive techniques based on test paper have been introduced, but they are less accurate and still require that blood be drawn. Accordingly, research has been conducted to address these problems.

It is desired to provide a method for measuring blood glucose concentration that is accurate and does not require the drawing of blood.

Therefore, it is an object of the present invention is to provide a non-invasive technique for measuring blood glucose concentration, that is to eliminate the need for drawing blood for this measurement.

A further object of the present invention is to provide a convenient, inexpensive, portable, easy-to-use apparatus for measuring blood glucose concentration.

SUMMARY OF THE INVENTION

The present invention is based on near-infrared radiation diffuse-reflection laser spectroscopy which measures blood glucose concentration by irradiating blood vessels with harmless electromagnetic radiation. This invention uses electromagnetic radiation of a wavelength that is transmitted through the skin to the measurement part, for example, a blood vessel. Since skin is mostly composed of water (H_2O), which absorbs IR radiation in nearly the entire IR spectral range, only radiation of a certain, narrow portion of the IR spectral range called the "water transmission window" will be transmitted through the skin.

Until recently, the water transmission window was thougth to only include wavelengths between 3~5μm. However, according to investigations by the present inventors, the wavelengths which is able to reach a blood vessel through the water transmission window includes wavelengths between 1.3~1.9μm.

Accordingly, the present invention uses electromagnetic radiation with a wavelength of 1.3μm~1.9μm radiation from a semiconductor diode laser. When electromagnetic radiation of these wavelengths irradiates the skin, ligth is transmitted through the skin to the blood vessel where the light interacts with the heterogeneous components of the blood. The light which reaches the blood is then diffusely reflected by the blood. The reflected light will have been modulated by the characteristic vibrations of the molecules which are major components of blood.

In the present invention, the diffusely reflected light described above is integrated by an integrating sphere. The photons ($h\nu$) integrated as described above, are converted into an electrical measurement value by a detector, and that value is supplied to a processing means, such as a one-chip microcomputer. The one-chip microcomputer calculates the blood glucose concentration using an accurate calibration method. Near-infrared radiation is defined in the present invention (in accordance with the International Union of Pure and Applied Chemistry (IUPAC) definition) as follows; frequency of about 10^{13}~3.75×10^{14}Hz; energy of about 0.951~35.8(Kcal/mol),0.0412~1.55eV; wavelength of about 0.8~30μm. The present invention is based on physical and chemical principles describing the vibrational motion of the blood glucose molecules as measured with near-infrared radiation diffuse-reflection laser spectroscopy. Such vibrational motion includes both rotational and translational motion, and includes overtone vibrations and combination vibrations. Of these vibrations, the overtone vibrations are dominant.

The analysis method incorporated in the present invention includes a mathematical model based on multiple linear regression analysis and multivariate analysis as modified by the present inventors to determine the blood glucose concentration.

The present invention provides a method and apparatus for measuring blood glucose concentration, which has the advantage of ease of use and

minimal expense for patients. The present invention has no consumable parts and is portable, allowing easy out-of-home testing. The present invention is more convenient than the prior art techniques. Also, this invention does not present the possible physical damage associated with the long-term use of syringes.

The measurement apparatus of the present invention can measure blood glucose concentration in a short time and unobtrusively. Therefore, the prior art techniques, with their inconvenience and expense are rendered obsolete.

The object and other objects of the present invention are achieved by measuring blood glucose concentration in a non-invasive technique, where:
a power source, for example, a battery is supplied to a one-chip microcomputer, a digtal display, a laser diode power supply, a detector (as needed), and an optical unit (as needed) by means of a power switch. The one-chip microcomputer controls the laser diode power supply so that it gradually applies current at a stable voltage and temperature to the laser diode, which emits the necessary wavelengths of radiation by means of a start/reset switch. The one-chip microcomputer is operated so that the D/A converter controlled by said one-chip microcomputer and driving said laser dioed power supply converts a digital control signal into an analog control signal.

Thus, the laser diode power supply causes the laser diode to emit a wavelength suitable for measurement. The light from said laser diode is collimated, or otherwise optically controlled, separated and combined. The optically controlled light is used to irradiate the skin adjacent to a blood vessel. The light absorbed, dispersed and diffusely reflected by the blood back through the skin is integrated by an integrating sphere. The photons collected by the integrating sphere are converted into an analog electrical signal with a detector. The analog electrical signal is transmitted to a preamplifier where the analog electrical signal is amplified. The amplified analog electrical signal is provided to an analog to digital (A/D) converter that converts the amplified analog electrical signal to a corresponding digital signal and outputs the digital signal to a one-chip microcomputer. The one-chip microcomputer calculates a blood glucose concentration from the digital signal by reference to a calibration curve stored in the memory of the one-chip microcomputer. The one-chip microcomputer causes the calculated blood glucose concentration to be displayed on a digital display.

An apparatus for measuring blood glucose concentration using a non-invasive technique according to the present invention comprises: one-chip microcomputer which controls the laser diode power supply so that current is gradually applied to a laser diode at a stable voltage and temperature. The one-chip microcomputer calculates the blood glucose concentration by comparing a detected value with a calibration curve stroed in memory of the one-chip microcomputer. A D/A converter converts the digital control signal output from said one-chip microcomputer into an analog control signal for control of the laser diode power supply that supplies power to the laser diode. The laser diode is a light source for the blood glucose concentration measurement. There may be a plurality of laser diodes for emitting light of different wavelengths or for emitting light of like wavelengths in accordance with the current supplied from the laser diode power supply. A temperature controller for controlling the temperature of the laser diode is connected between the laser diode power supply and the laser diode. An optical unit collimates the light emitted from the laser diode, or optically controls, separates and combines the light from the laser diode. An integrating sphere integrates the light dispersed and diffusely reflected from the blood when the blood is illuminated through the skin by light from the optical unit. A detector for converts the photons collected by the intergrating sphere into an analog electrical value which is then amplified in the preamplifier. An A/D converter converts the electrical analog measurement value into a digital value. A digital display displays the blood glucose concentration calculated by the one-chip microcomputer.

BRIEF DESCRIPTION OF THE DRAWINGS

These and other objects and features of the present invention will be understood through the various embodiments by reference to the accompanying drawings in which:

Figure 1 is a block diagram showing an apparatus for measuring blood glucose concentration according to the present invention; and

Figure 2 is a detailed circuit diagram showing the apparatus for Figure 1.

DETAILED DESCRIPTION OF THE INVENTION

A preferred embodiment of a measurement apparatus according to the present invention will be described hereinafter with reference to the accompanying drawings.

Referring to Figure 1, when a power switch 1 is switched ON, a power is supplied from the battery (generally 4.5~9V and is suited to a charging battery of 6V among other possibilities) to a one-chip

microcomputer 2. At the same time, the power source is supplied to a digital 3, a laser diode power supply 4, and optical unit 6 (as needed).

If the start/reset switch 8 is then switched ON, the laser diode power supply 4 supplies the laser diode 5 with power in accordance with the control signal supplied by the one-chip microcomputer 2. As a result, the laser diode current gradually increases if the current exceeds the threshold current (approximately 20mA). Thus, laser diode 5 starts emitting light.

The laser diode 5 emits light (for example, light having a wavelength of 1.3μm~1.9μm, and light having a wavelength of 1.4μm~1.8μm, among others), of a wavelength necessary for blood glucose concentration measurement. This wavelength is achieved by gradually increasing the current supplied with in the range of approximately 20~200mA at a stable voltage and temperature in accordance with the characteristics of the laser diode. In the present invention, the laser diode 5 is composed of between 1 and 30 diodes, and each may emit light of a different wavelength, or each may emit light of the same wavelength.

The light emitted from the collective diodes in the laser diode 5 may be simultaneously emitted by the diodes or sequentially emitted by each diode. In case of simultaneous operation, length will be selected, for example, using the Fourier Transform.

The light outputted from the collective diodes of the laser diode 5 is supplied to an optical unit 6, and collimated, or the light is optically controlled, separated and combined. Thereafter, the light is passed through an integrating sphere 9 and divided in one or more directions.

The light which passes through the integrating sphere 9 is successively irradiated to the skin of a subject, or is successively irradiated to a reference port which was ready beforehand as the case may be. Here, the reference port is not necessarily needed.

The light absorbed, dispersed and diffusely reflected from the blood is detected by a detector 7 after being integrated by means of the integrating sphere 9. The integrating sphere is of a globular or like shape. Here, the size of integrating sphere 9, which is integrated with light dispersed and reflected from the blood, has a width, length and height under 2.56cm, and is suitable for under 1.28cm, and more particularly, is suitable for under 0.64cm.

An electrical analog measurement value detected as above described is amplified by a preamplifier connected to the detector 7. Thereafter, the electrical analog measurement value is converted into a digital measurement value by means of an A/D converter 11.

Next, the one-chip microcomputer 2 calculates and computes the measured value by comparing the signal converted into a digital measurment value by the A/D converter 11 with a calibration curve stored in memory of the one-chip microcomputer 2. The resultant value is displayed on the digital display 3.

The dimensions of the above-described apparatus may be: width×length×height under 170mm×80mm×25mm, and is suitable for under 150mm×75mm×22mm, among others, and more particularly, is suitable for under 130mm×70mm×20mm.

A photo diode is suitable as the detector 7 and may be a Ge detector, and more particularly, may be a Ge detector connected to a preamplifier. Moreover, the optical unit 6 is composed of components which constitute a light which has a diameter under 0.5~5mm (under 2mm among others) in order to condense and diffuse the light in parallel.

Furthermore, the present invention is not limited to an integrating sphere 9 having a globular or like shape, but it may also be of an oval or a half-oval or different shape.

In the present invention, the port can be separated from the above measurement apparatus. In this case, the light emitted from the laser diode 5 can be transmitted to the port through the optic fiber, and the distance between the port and the measurement apparatus is 100~1,000mm and is suitable for 500mm among others, and more particularly, may be 300mm. Of course, the port cannot be separated from the measurement apparatus.

The present invention is not limited for one-chip microcomputer 2 separated from the D/A converter 10 and the A/D converter 11, but can also be a one-chip microcomputer 2 which is included in the D/A converter 10 and the A/D converter 11.

Moreover, in the present invention, it can be used with auxiliary circuit 12 which is composed of RAM 12_1 and EPROM 12_2 in order to aid an operation of one-chip microcomputer 2.

The present invention is not limited for the measurement of blood glucose concentration and, for example, can be applied to a measurement of a cholesterol concentration or an alcohol concentration.

According to the present invention as above described, there is provided an economic method and apparatus for measuring blood glucose concentration in a non-invasive technique, which can easily measure the blood glucose concentration by putting port of the apparatus to a certain part of the human body sight of a blood vessel without using an equipment, such as a conventional injector.

Claims

1. A method for measuring the concentration of a chemical carried in the blood stream including the steps of irradiating a blood vessel with a laser diode near-infrared light source, detecting with a photodetector radiation dispersed or diffusedly reflected by the blood in the blood vessel, and analysing the output of the photodetector to determine the concentration, in the step of irradiating the blood vessel the vessel being irradiated at a wavelength in the range from substantially 1.3μm to substantially 1.9μm.

2. A method according to claim 1 in which the chemical concentration measured is blood glucose concentration, the method comprising the steps of:
supplying a power source from a battery to a processing means, a digital display, a laser diode power supply, a detector and an optical unit by means of a power switch;
controlling said processing means so that said laser diode power supply gradually applies current to said laser diode at a stable voltage and temperature by means of start/reset switch;
controlling said processing means so that a D/A converter coupled between said processing means and said laser diode power supply converts a digital control signal into an electrical control signal;
emitting a wavelength sufficient for measurement in said laser diode by means of said laser diode power supply;
callimating the light emitted from the laser diode parallel to a corresponding object, or optically controlling, separating and combining the light emitted from said laser diode;
irradiating through an integrating sphere said optically controlled light to a blood vessel to measure blood glucose concentration;
integrating by means of said integrating sphere the light absorbed, dispersed and diffusely reflected by the blood after the light reaches the skin to the blood;
transmitting the signal amplified by a preamplifier connected to said detector to an A/D converter, after converting photons integrated by said integrating sphere and detected by said detector into an electrical analog measurement value the step of analysing the output comprising:
transmitting the signal to said processing means, after converting said electrical analog measurement value into a digital measurement value by means of said A/D converter;
calculating and computing blood glucose concentration by comparing a calibration curve stored in memory region of said processing means with a digital measurement value converted by said A/D converter;
displaying a calculated blood glucose concentration on said digital display.

3. A method for measuring blood glucose concentration according to claim 1 or 2, wherein said measurment method is based on physical and chemical principles of vibrational motion of blood glucose molecules in nesr-infrared radiation diffuse-reflection laser spectroscopy due to vibrational, rotational and translational motion, utilizing overtone vibrations and a combination of other types of vibrations.

4. A method for measuring blood glucose concentration accoring to claim 2 or 3, wherein in the step of calculating and computing blood glucose concentration by comparing a calibration curve stored in the memory of said processing means with a digital measurement value converted by said A/D converter, utilizes a mathematical method such as a multiple linear regression analysis and a multivariate analysis.

5. An apparatus for measuring blood glucose concentration comprising;
processing means for controlling the flow of current supplied from a laser diode power supply to a laser diode so that current is applied gradually and at stable voltage and temperature levels, said processing means for calculating and computing blood glucose concentration by comparing and electrical analog measurement value detected and converted by a detector with a calibration curve stored in a memory of said processing means;
a D/A converter for controlling the laser diode power supply by converting a digital control signal to an analog control signal, wherein said laser diode power supply applies a power source to said laser diode as a light source for blood glucose concentration measurement, and said laser diode consisting of a plurality of diodes for emitting light of different wavelengths or emitting light of the same wavelengths, in accordance with the current supplied from said laser diode power supply;
a temperature controller which controls the temperature of said laser diode, said temperature controller being connected between said laser diode power supply and said laser diode;
an optical unit which collimates light emitted from said laser diode parallel to corresponding object and optically controls, separates or combines the light emitted from said laser diode;
an integrating sphere which integrates light dispersed and diffusely reflected from the blood by irradiating light controlled by said optical unit to the skin of a diabetics as a measurement part;
a detector which amplifies a signal by means of a preamplifier connected its own after converting photon integrated by said integrating sphere into an electrical analog measurement value; and
an A/D converts said electrical analog measurement value into a digital measurement value; and
a digital display for displaying the calculated and

computed blood glucose concentration.

6. An apparatus for measuring blood glucose concentration according to claim 5, wherein the wavelength of the electromagnetic radiation emitted from said laser diode is in the near-infrared region, and is 1.3 to 1.9μm among others, and more particularly, is 1.4 to 1.8μm, and
the light emitted from said laser diode simultaneously irradiates the blood through the skin, or sequentially irradiates the blood through the skin.

7. An apparatus for measuring blood glucose concentration according to claim 5 or 6, wherein said integrating sphere is globular or like shape, oval or half oval or different shape, and
said integrating sphere has a width, length and height under 2.56cm, and is suitable for under 1.28cm among others, and more particularly, is suitable for under 0.64cm, and
said measurement apparatus has a width×length×height under 130mm×70mm×20mm, and is suitable for under 150mm×75mm×22mm among others, and more particularly, is suitable for under 130mm×70mm×20mm.

8. An apparatus for measuring blood glucose concentration according to claim 5, 6 or 7 wherein said port can be separated from the measurement apparatus by means of an optic fiber, and the distance between port and measurement apparatus is 100~1,000mm, and is suitable for 500mm among others, and more particularly, is suitable for 300mm.

9. An apparatus for measuring blood glucose concentration according to claim 5, 6, 7 or 8 wherein a photo diode is utilized as said detector which detects photons integrated by said integrating sphere, and is utilized a Ge detector, and more particularly, is utilized a Ge detector coupled to a preamplifier, and
said D/A converter and A/D converter are separated from said processing means, or are included in said processing means, and
said battery used as a power source is 4.5 to 9V, and is suitable for a charging battery of 6V among others.

FIG.1.

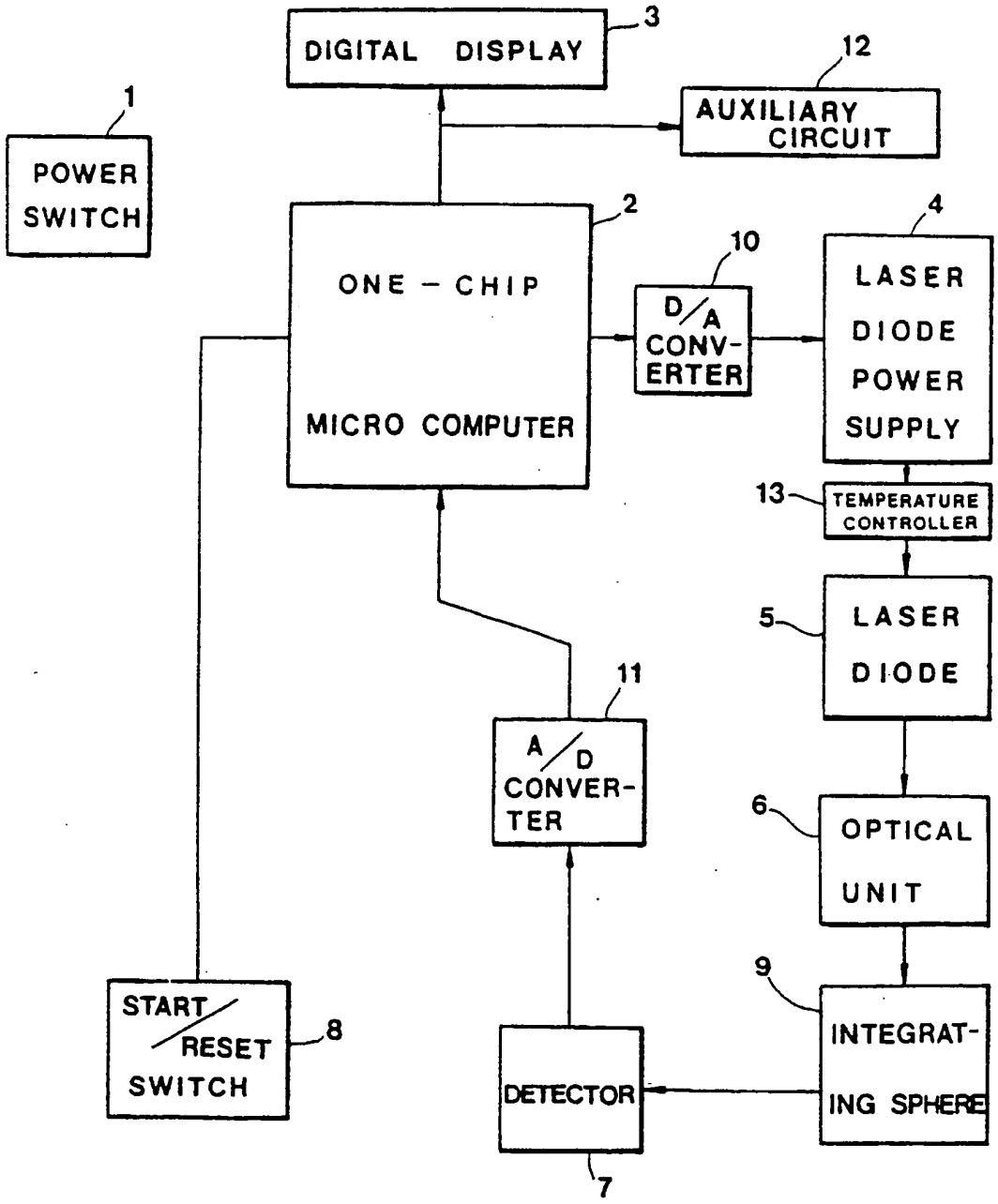
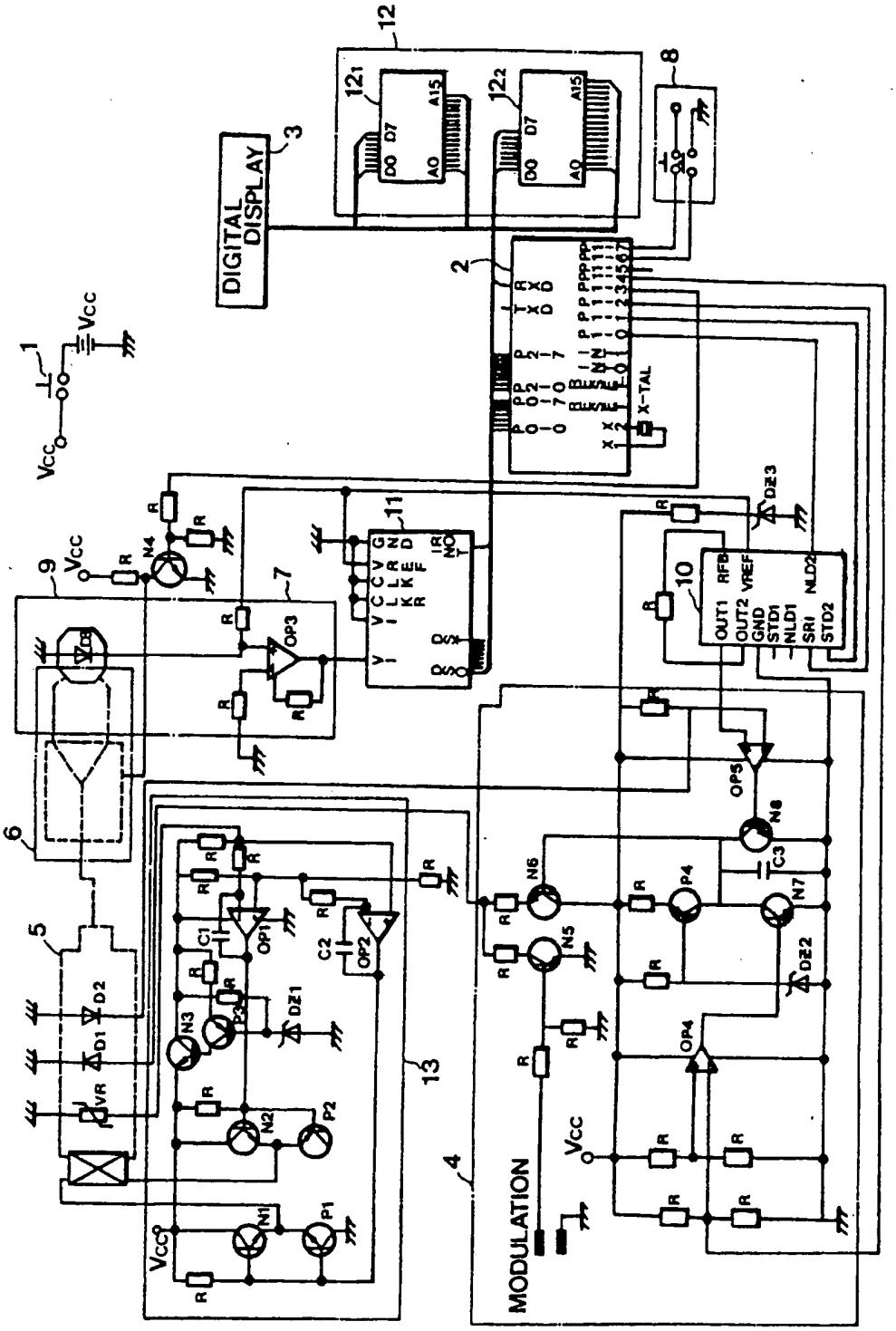

DIGITAL DISPLAY
3
12
AUXILIARY CIRCUIT
1
POWER SWITCH
2
ONE - CHIP
MICRO COMPUTER
10
D/A CONV-ERTER
4
LASER DIODE POWER SUPPLY
13
TEMPERATURE CONTROLLER
5
LASER DIODE
11
A/D CONVER-TER
6
OPTICAL UNIT
9
INTEGRAT-ING SPHERE
START/RESET SWITCH
8
DETECTOR
7

FIG.2.


DIGITAL DISPLAY
MODULATION
X-TAL
OUT1
OUT2
GND
STD1
NLD1
SRI
STD2
RFB
VREF
NLD2

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EUROPEAN SEARCH REPORT

Application Number

EP 90 31 1596

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
Y,A	EP-A-0 317 121 (KURASHIKI BOSEKI K. K.) * figures * * column 5, line 25 - page 11, line 36 *	1,2,5,7,9	A 61 B 5/00
Y,A	EP-A-0 074 428 (MÜLLER) * figures 3-6, 9 * * page 17, line 13 - page 26, line 31 * * page 29, line 18 - page 31, line 12 *	1,2,5,9	
A	EP-A-0 160 768 (BATTELLE MEMORIAL INSTITUTE) * figures 1-3 * * page 4, line 30 - page 14, line 30 *	1,2,5,9	
A	EP-A-0 274 403 (WHATMAN REEVE ANGEL PLC) * figures 1, 6 * * page 3, line 1 - page 4, line 17 * * page 5, lines 43 - 50 *	1,2,5,7-9	
A	DE-A-3 328 862 (SIEMEMS AG) * figures * * page 7, line 13 - page 13, line 25 *	1,2,4,5	
A	APPLIED SPECTROSCOPY. vol. 43, no. 5, July 1989, BALTIMORE US pages 834 - 839; MAY: "Computer processing of tunable diode laser spectra." * page 835; figure 1 *	2,5	

TECHNICAL FIELDS SEARCHED (Int. Cl.5)

A 61 B
G 01 N

The present search report has been drawn up for all claims

Place of search	Date of completion of search	Examiner
The Hague	11 February 91	CHEN A.H.

CATEGORY OF CITED DOCUMENTS

X: particularly relevant if taken alone
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A: technological background
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